Award Number: W81XWH-15-1-0614

TITLE: Biomarkers of Spontaneous Recovery from Traumatic Spinal Cord Injury

PRINCIPAL INVESTIGATOR: Ona Bloom

CONTRACTING ORGANIZATION: The Feinstein Institute for Medical Research
Manhasset, NY 11030

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Ona Bloom, PhD (PI)

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The Feinstein Institute for
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350 Community Drive
Manhasset, NY 11030

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14. ABSTRACT

Immediately after SCI, a person confronts 3 major questions: (1) how much function have they lost, (2) what treatments promote recovery, (3) how much physical recovery can they expect over time? To answer the first question, a clinical exam tests motor and sensory function throughout the body. The second question is still largely unanswered: standard rehabilitation focuses on maximizing preserved function and managing medical complications of living with SCI. Currently, there is no FDA-approved drug to promote recovery after SCI. The third question is also unanswered; there is no standardized model to predict functional recovery, which occurs mostly within the first year after SCI. Surprisingly little is known about the biological processes influencing recovery after SCI. Experiments indicate that inflammation worsens the initial area of damage and inhibits physical recovery. Signs of inflammation occur in people newly injured and in people living with SCI for many years. Our hypothesis is that some inflammatory factors are higher in individuals with SCI that achieve less physical recovery. We are performing a prospective, longitudinal study to measure circulating biochemical responses and functional recovery throughout the 1st year after SCI, within the same individuals. Data will be used to derive a predictive, multiscale model of functional recovery after SCI. The goal is to build an easy-to-implement, predictive model of functional recovery after SCI that incorporates biomarkers related to inflammation.

15. SUBJECT TERMS

traumatic spinal cord injury, spinal cord, spontaneous recovery, functional recovery, inflammation, biomarkers, trauma

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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1. **INTRODUCTION:** Immediately after a traumatic spinal cord injury (SCI), a person confronts 3 major questions: (1) how much function have they lost, (2) what treatments promote recovery, and (3) how much physical recovery can they expect over time? To answer the first question, a clinical exam tests motor and sensory function throughout the body. The second question is still largely unanswered: standard rehabilitation focuses on maximizing preserved function and managing medical complications of living with SCI. Currently, there is no FDA-approved drug to promote recovery after SCI. The third question is also unanswered; there is no standardized model to predict functional recovery, which occurs mostly within the first year after SCI. Surprisingly little is known about the biological processes influencing recovery after SCI. Experiments indicate that inflammation worsens the initial area of damage and inhibits physical recovery. Signs of inflammation occur in people newly injured and in people living with SCI for many years. Our hypothesis is that some inflammatory factors are higher in individuals with SCI that achieve less physical recovery. To test this hypothesis, we are performing a multi-site prospective, longitudinal study to measure circulating biochemical responses and functional recovery throughout the 1st year after SCI, within the same individuals. Data will be collected at least once within 0-3 days post injury (dpi), and then at 3, 6, and 12 months after SCI. The goal is to use these data to build an easy-to-implement, predictive multi-scale model of functional recovery after SCI that incorporates biomarkers related to inflammation.

2. **KEYWORDS:**

traumatic spinal cord injury, spinal cord, inflammation, biomarkers, spontaneous recovery, functional recovery, trauma

3. **ACCOMPLISHMENTS:**

- **What were the major goals of the project?**

The major goals, as stated in the original Statement of Work (SOW), are described below.
Site 1: The Feinstein Institute for Medical Research (of Northwell Health),
Site 2: Kessler Foundation,
Site 3: University (Univ.) of Louisville.

Major Task 1: Obtain IRB and HRPO/ACURO permission for study
Subtask 1: Submit documents for local IRB review
Subtask 2: Submit IRB approval and necessary documents for HRPO review

Major Task 2: Create Infrastructure and Obtain All Supplies/Training for Performance of Outcome Measures
Subtask 1: Instruction or Review of Functional Outcome measures.
Subtask 2: non-NRN site personnel visit NRN site(s) for observational case study learning.
Subtask 3: Create custom clinical database for data entry
Subtask 4: Create SOP for clinical team, including data entry forms and instruction on use
Subtask 5: Send sample collection supplies, SOP and shipping supplies to all sites

Major Task 3: Human Subject Study Enrollment
Subtask 1: Recruit, consent and enroll subjects at acute time points, study visit 1
Subtask 2: Obtain Biological Samples (blood) from subjects, study visits 1-4
Subtask 3: Process and store biological samples, study visits 1-4
Subtask 4: Perform ISNCSCI exams and determine AIS grades
Subtask 5: Administer SCIM and determine scores, study visits 2-4
Subtask 6: Administer NRS and determine scores, study visits 2-4

Major Task #4: Data Analysis, Modeling and Interpretation
Subtask 1: Pilot Study: Perform biochemical assays on biological samples from subset of subjects
Subtask 2: Pilot Study: Perform data analysis, statistical modeling and interpretation of data
Subtask 3: Larger/Complete Set of Study Samples: Perform biochemical assays on biological samples from subset of subjects

- **What was accomplished under these goals?**

1) Major Activities:
Major activities were focused on making progress within Major Task 3, Human Subject Study Enrollment. By holding monthly conference calls between all sites to discuss study related issues, we realized early in Year 2 that as with many acute traumatic SCI studies, recruitment and retention of participants had become a significant challenge.

At Site 1, we initiated several new efforts aimed to increase recruitment and retention, which are still ongoing: To increase screening, we instituted receipt of electronic daily alerts for ICD10 codes relevant to patients admitted with a possible traumatic SCI. In addition to daily in-person communication with key personnel at our level 1 trauma center, we also initiated screening from a level 2 trauma center within our health system. To increase retention, we now offer to conduct study visits at home if a participant prefers, we established better communication with study participants between visits, and we arranged for local participant travel to study visits.

In February 2017, key study personnel from all sites agreed that in order to meet the recruitment goals of the study, additional study sites should be added and an extension of the study period requested. With advice and guidance from the DOD Science Officer, the PI recruited 3 additional sites with significant expertise in acute SCI:
Site 4- Thomas Jefferson University (PI: James Harrop MD)
Site 5- University of British Columbia (PI: Brian Kwon MD/PhD)
Site 6- Ohio State University Medical Center (PI: Jan Schwab MD/PhD)

On May 22, 2017 the PI submitted a request to extend the project period for one year, which included a revised Statement of Work (SOW) dated 20170519, with the additional sites specified and new projected participant enrollment table. The request and a modification to the contract were granted, effective as of August 17, 2017. Therefore, this annual report will cover both the initial and revised SOW goals, along with the justification of the modification, as indicated below.

2) Specific Objectives of the Project:
- Major Task 1 was accomplished at Sites 1, 2, 3. Local IRB approval is now being initiated at Sites 4, 5, 6. As soon as it is obtained, HRPO approval will be sought.
- Major Task 2 was accomplished at Sites 1, 2, 3. It is now initiated at Sites 4, 5, 6.
- Major Task 3 was accomplished at Sites 1, 2, 3. We will initiate this at Sites 4, 5, 6 as soon as local IRB and HRPO approval are obtained. Data below is therefore for Sites 1, 2, 3 only:
    - Year 1: a combined total of 29 participants were screened and 5 were enrolled.
    - Year 2: a combined total of 103 participants were screened and 9 were enrolled.
    - Total year 1 + 2: a combined total of 132 participants were screened and 14 were enrolled.

3) Significant or key outcomes: major findings, developments or conclusions:
As described above, the major development of Year 2 was to experience challenges in recruitment and retention. We then sought solutions to those challenges. We believe that the addition of 3 new sites will enable us to accomplish our initial project goals.

4) Other achievements:
What opportunities for training and professional development has the project provided?

Enhanced Scientific Exchange via Site Visits: To enhance coordination between sites and to provide additional opportunities for scientific exchange related to SCI research, Dr. Bloom, (PI) made site visits to The Kessler Foundation (Site 2), where she met with Dr. Forrest and key study personnel (Feb. 24, 2017) and to the Univ. of Louisville (Site 3), where she met with Dr. Boakye, Dr. Harkema and other key study personnel (June 7-9). To recruit the new sites 4, 5, 6, Dr. Bloom hosted Dr. Jan Schwab (Site 6: OSUMC) at her institution (July 12-14), and visited with Dr. Harrop and other key study personnel at their site (Site 4: Thomas Jefferson). From March-present, Dr. Bloom communicated by phone and email with Dr. Kwon and other key study personnel at his site (Site 5: ICORD/UBC).

Professional Development:
- As in Year 1, Dr. Bloom and other key study personnel attended several professional conferences to present other SCI related work ongoing in their labs and to learn about other efforts ongoing and topics of interest related to this

study. Below are examples of such activities for Dr. Bloom: (Travel to these meetings was not funded by the DOD):

- November, 2016 Annual meeting of the Society for Neuroscience (SFN)
- February, 2017 Annual meeting of the Association of Academic Physiatrists (AAP)
- April, 2017 Annual meeting of the American Spinal Injury Association (ASIA)
- September, 2017 19th Spinal Research Network Meeting, International Spinal Research Trust (ISRT)

Training Opportunity:

- The New York State Dept. of Health recently re-instated its Spinal Cord Injury Research Board (NYSCIRB), which supports SCI related research within NY State. This year, they have had several RFAs that the PI was eligible to apply for because of this DOD funded study:
    - Individual Predoctoral and Postdoctoral Fellowships in SCI Research (round 2): This RFA supports 3 years of training (salary) for an early stage postdoctoral fellow to be mentored by a PI with SCI funded research. One of the mentoring activities included in the Bloom Lab application was the opportunity to use the DOD study to introduce a trainee to human subject research, the SCI specific outcome measures and the biological data analysis methods. The trainee will then apply this training to initiate a pilot study of biomarkers in pediatric patients with acute SCI, in partnership with our health system's level one pediatric trauma center at Cohen Children's Medical Center. The application was funded and initiated 9/1/2017. Candidate fellows are currently being screened for this position.
    - Institutional Support for SCI Research (Round 6: Non-competitive Funding Opportunity): This RFA provides 5 years of institutional support to expand existing SCI research projects or to establish new ones. In order to qualify for this RFA, the PI must have federally funded SCI related research, directly enabled by this DOD grant. The DOD funded Aim 1 is to perform: a) multiplex immunoassays to determine elevated inflammatory proteins in blood; b) microarray analysis of mRNA from whole blood. At Site 1 only, some of the NYSCIRB funds we requested here will support expansion of the immune outcome measures to include analysis of circulating immune cells (by multicolor flow cytometry) and to collection/analysis of additional acute biological samples, as the DOD programmatic reviewers had originally requested. These samples, which may be obtained from as early as the day of SCI, may enhance the scope and impact of the study. The application was funded and initiated 3/1/2017.

How were the results disseminated to communities of interest?

Although we do not yet have results from this study, Dr. Bloom (PI) presented the scientific background, study design and goals at a seminar in the Department of Physiology, Emory University, Atlanta, GA (March, 2017).

Dr. Bloom (PI) also presented the scientific background, study design and goals at Grand Rounds, Department of Physical Medicine and Rehabilitation Grand Rounds, Glen Cove Hospital, Northwell Health, Glen Cove, NY (October 2016).

- **What do you plan to do during the next reporting period to accomplish the goals?**

  After subcontracts are executed with the 3 new sites, they will join our original 3 sites to follow the scheduled list of tasks stated on the Statement of Work revised 20170519:

Major Task 1: Obtain IRB and HRPO/ACURO permission for study (Sites 4-6)
Subtask 1: Submit documents for local IRB review
Subtask 2: Submit IRB approval and necessary documents for HRPO review

Major Task 2: Create Infrastructure and Obtain All Supplies/Training for Performance of Outcome Measures (Sites 4-6)
Subtask 1: Instruction or Review of Functional Outcome measures.
Subtask 2: non-NRN site personnel visit NRN site(s) for observational case study learning.
Subtask 3: Create custom clinical database for data entry
Subtask 4: Create SOP for clinical team, including data entry forms and instruction on use
Subtask 5: Send sample collection supplies, SOP and shipping supplies to all sites

Major Task 3: Human Subject Study Enrollment (Sites 1-6)
Subtask 1: Recruit, consent and enroll subjects at acute time points, study visit 1

Subtask 2: Obtain Biological Samples (blood) from subjects, study visits 1-4
Subtask 3: Process and store biological samples, study visits 1-4
Subtask 4: Perform ISNCSCI exams and determine AIS grades
Subtask 5: Administer SCIM and determine scores, study visits 2-4
Subtask 6: Administer NRS and determine scores, study visits 2-4

Major Task #4: Data Analysis, Modeling and Interpretation (Sites 1-6)
Subtask 1: Pilot Study: Perform biochemical assays on biological samples from subset of subjects
Subtask 2: Pilot Study: Perform data analysis, statistical modeling and interpretation of data
Subtask 3: Larger/Complete Set of Study Samples: Perform biochemical assays on biological samples from subset of subjects

4. IMPACT:

- **What was the impact on the development of the principal discipline(s) of the project?** Nothing to report.
- **What was the impact on other disciplines?** Nothing to report.
- **What was the impact on technology transfer?** Nothing to report.
- **What was the impact on society beyond science and technology?** Nothing to report.

5. CHANGES/PROBLEMS:

- **Changes in approach and reasons for change**

As described above, we received permission from the DOD to extend the study for an additional year and to add 3 additional sites. The reason for this was continued challenges with recruitment and retention, which we hope will be mitigated by our inclusion of additional sites of excellence from within the SCI research community.

- **Actual or anticipated problems or delays and actions or plans to resolve them**

As described above, we made several new efforts at Site 1 aimed to increase recruitment and retention, which are still ongoing. We now have a revised SOW (dated 20170519), to add 3 new sites to the study. This effort to enable all sites to become active in the study is now ongoing. Screening, recruitment and retention is ongoing at the 3 original sites.

- **Changes that had a significant impact on expenditures**

As mentioned above, we have added 3 new recruitment sites with no change to the total cost of the project. In order to accommodate the new SOW, we submitted plans for a revised budget. The Modification of the Contract (P00001) was approved effective August 17, 2017, included the following yearly budgets:
Year 1 $499, 536
Year 2 $582, 625
Year 3 $594, 734
Under the modified budget, at each site, a site PI and key personnel will be paid for their efforts related to study initiation, maintenance, and participant screening. Sites will be paid additional fees for their study related costs on a per-participant-recruited basis. Based on estimates from the new site PIs and revised estimates from the original site PIs, an expected recruitment table was included in the SOW 20170519. However, as stated in the request for project modification and extension, some sites may over- or under-perform their predicted enrollment. Therefore, each site will submit invoices to the overall PI (Dr. Bloom) for costs of recruiting actual participants. This will enable us to accommodate expenses incurred at all 6 sites.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents-**Not applicable.
- **Significant changes in use or care of human subjects -**Not applicable.
- **Significant changes in use or care of vertebrate animals-**Not applicable.
- **Significant changes in use of biohazards and/or select agents-**Not applicable.

6. PRODUCTS:

- **Publications, conference papers, and presentations.**

- **Journal publications.** Nothing to Report
- **Books or other non-periodical, one-time publications.** Nothing to Report
- **Other publications, conference papers, and presentations.**
  As stated above, Dr. Bloom (PI) presented the scientific background, study design and goals on 2 occasions:
  Departmental Seminar, Department of Physiology, Emory University, Atlanta, GA (March, 2017).

  Grand Rounds, Department of Physical Medicine and Rehabilitation Grand Rounds, Glen Cove Hospital, Glen Cove, NY (October, 2016).

- **Website(s) or other Internet site(s)**: This study is listed on clinicaltrials.gov:

https://clinicaltrials.gov/ct2/show/NCT02731027?term=biomarkers+of+spinal+cord+injury&rank=2

- **Technologies or techniques-**Not applicable**.**
- **Inventions, patent applications, and/or licenses-** Not applicable**.**
- **Other Products-**Not applicable.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

- **What individuals have worked on the project?**

What Individuals have worked on the project? ≥ 1 person month this year	Site 1: Feinstein Institute for Medical Research
Name:	Ona Bloom, PhD
Project Role:	Overall PI
Researcher Identifier (e.g. ORCID ID):	0000-0002-8340-2392
Nearest person month worked:	3
Contribution to Project:	Dr. Bloom is responsible for overseeing all aspects of the project, supervises and participates in all on-site tasks and Site 1 personnel, and coordinates between study sites.
Funding Support:	DOD (3 calendar months), NY State Spinal Cord Injury Research Board, institutional support round 6, and institutional support. She is also supported by NIAMS for another project.
Name:	Matthew Bank, MD
Project Role:	Co-investigator, Site 1, (No Change from original submission)
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	
Contribution to Project:	Dr. Bank is responsible for the identification of acute SCI patients at the local trauma center. He is present during the consent process and is available during the participants' acute hospital length of stay.
Funding Support:	DOD (this grant). He is also supported by departmental funding.

Name:	Adam Stein, MD
Project Role:	Co-investigator, Site 1, (No Change from original submission)
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	
Contribution to Project	Dr. Stein is responsible for the evaluation of study participants in the visits following hospital discharge.
Funding Support:	DOD (this grant). He is also supported by departmental funding.
Name:	Martin Lesser, PhD
Project Role:	Director, Biostatistics Unit, Site 1, (No Change from original submission)
Researcher Identifier (e.g. ORCID ID):	0000-0002-0318-5739
Nearest person month worked:	
Contribution to Project:	
Funding Support:	DOD (this grant). He is also supported by NIH and departmental funding for work on other projects.
Name:	Cristina Sison, PhD
Project Role:	Assistant Director, Biostatistics Unit, Site 1
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	
Contribution to Project:	
Funding Support:	DOD (this grant). She is also supported by NIH and departmental funding for work on other projects.
Name:	James Tsang
Project Role:	Biostatistics Support
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1.2
Contribution to Project:	Supervised by Dr. Lesser, created and is maintaining the custom clinical database, developed plans for data monitoring, data management and reporting
Funding Support:	DOD (this grant). He is also supported by NIH grants and departmental funding for work on other projects.
Name:	Rachel Monahan
Project Role:	Research Coordinator
Researcher Identifier	

(e.g. ORCID ID):	
Nearest person month worked:	6
Contribution to Project:	Ms. Monahan submitted and maintained local IRB regulatory binder and correspondence, maintained all HRPO/ACURO related documents and correspondence, participated in development of case report forms, input data to clinical database, performed sample processing, biochemical assays shipped supplies to other sites, coordinated communication with other sites (monthly conference calls), trained other site personnel on how to use database for submitting data and participated in data analysis.
Funding Support:	DOD (this grant). NY State Spinal Cord Injury Research Board, institutional support round 6 and institutional funds for this and other projects.
Name:	Ashley Chory
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	4
Contribution to Project:	Ms. Chory assumed the roles and responsibilities previously provided by Ms. Monahan.
Funding Support:	DOD (this grant). NY State Spinal Cord Injury Research Board, institutional support round 6 and institutional funds for this and other projects.
What Individuals have worked on the project? ≥ 1 person month this year	Site 2: Kessler
Name:	Gail Forrest, PhD
Project Role	Site 2 (Kessler) PI (No Change from Initial Submission)
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1.2
Contribution to Project:	Dr. Forrest is responsible for overseeing this project at site 2, supervises site 2 personnel, and participates in all on-site tasks.
Funding Support:	DOD (This project) She is also supported by NJCSCR, USAMRAA, NIH and departmental funding.
Name:	LeighAnn Martinez
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2.4
Contribution to Project:	Ms. Martinez submitted and maintained local IRB regulatory binder and correspondence and related documents, participates in monthly study personnel conference calls
Funding Support:	DOD (this project). For other projects, she is supported by: NJCSCR, NIH, NIDILRR.

What Individuals have worked on the project? ≥ 1 person month this year	Site 3: University of Louisville
Name:	Max Boakye, MD (No Change from original submission)
Project Role:	Site 3 (Univ. of Louisville) PI (No change from original submission.)
Researcher Identifier (e.g. ORCID ID):	0000-0002-1758-9136
Nearest person month worked:	1.2
Contribution to Project:	Dr. Boakye is responsible for overseeing this project at site 3, supervises site 3 personnel, and participates in all on-site tasks.
Funding Support:	DOD (this grant). He is also supported by Helmsley trust grants and departmental funding for work on other projects.
Name:	Debra Williams
Project Role:	Research Coordinator (No change from original submission.)
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	Ms. Williams submitted and maintained local IRB regulatory binder and correspondence and related documents, submitted data for case report forms to custom database, participates in monthly study personnel conference calls.
Funding Support:	DOD (this grant). She is also supported by Reeve foundation grants and departmental funding for work on other projects.
Name:	Yukishia Austin (No Change from original submission)
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	Ms. Austin participated in screening participants, research coordination, collecting data for case report forms and submitting them to custom database, participates in monthly study personnel conference calls
Funding Support:	DOD (this grant). She is also supported by departmental funding for work on other projects.
Name:	Lori Clark
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	Ms. Clark participates in screening participants, research coordination, collecting data for case report forms and submitting them to custom

	database, participates in monthly study personnel conference calls
Funding Support	DOD (this grant). She is also supported by Reeve foundation grants and departmental funding for work on other projects.

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Note: For all personnel listed below, the information provided is in addition to this DOD grant "*Biomarkers of Spontaneous Recovery from Traumatic Spinal Cord Injury".*

Site 1: Feinstein Institute for Medical Research

Ona Bloom PhD, Principal Investigator (Feinstein Institute):

Active Support:
National Institutes of Health (NIH) 1R01AR069668-01 Chahine (PI) 09/1/2017-03/31/2022
Mechanobiology of Inflammation in the Intervertebral Disc.
Disability and pain from degenerated intervertebral discs (IVD) affects >40% of U.S adults, costs >$100 billion annually and the etiology is unknown. The aim of this study is to investigate the mechanobiology of the inflammatory cytokine high mobility group box 1 protein (HMGB1) signaling in the pathophysiology and mechanotransduction of the intervertebral disc
Role: Co-Investigator, 0.6 Calendar Months, (5%).

New Active Support:
NY State Spinal Cord Injury Research Board (NYSCIRB) DOH01-ISSCI6-2016-00018 Bloom (PI) 3/1/2017-2/28/2022 *Institutional Support for SCI Research, round 6*.
This is a grant to support expansion of 3 separate, ongoing projects that aim to improve our understanding of factors that influence physical recovery and wellness in persons with spinal cord injury (SCI). The Projects are: (1) "*Biomarkers of Spontaneous Recovery from Traumatic SCI*," (2) "*Biomarkers in Pediatric Spinal Cord Injury/Abnormalities*," and (3)"*Strive for Wellness Research Outcomes*," Project 1 is supported by the US DOD. Funding is provided here for non-overlapping aims. Projects 2 and 3 are not supported by any other external funds.
Role: Principal Investigator, 3 Calendar Months, (25%)

NY State Spinal Cord Injury Research Board (NYSCIRB) DOH01-FLLOW2-2016 Bloom (PI) 09/01/2017-8/31/2020
Individual Predoctoral and Postdoctoral Fellowships in Spinal Cord Injury Research (round 2).
This is a training grant awarded to support the salary of a postdoctoral fellow to enter and receive training in the field of spinal cord injury. There is no PI salary support.

Pending (recommended for funding, notice of award not yet received):
NY State Spinal Cord Injury Research Board (NYSCIRB) DOH01-PART2-2017-00069 Bloom (PI) 11/01/2017-10/31/2019
Impact of Walking on the Immune System of person with chronic spinal cord injury.
The aims of the project are to measure the systemic inflammatory mediators and profile leukocyte transcriptional responses in participants with chronic SCI before and after 12 weeks of overground walking in an exoskeleton. Participants will be recruited from an ongoing study led by Dr. Ann Spungen, JJPVAMC.
Role: Principal Investigator, 0.6 Calendar Months, (5%)

Martin Lesser PhD, Key Personnel
New Active Support: None

New Completed Support
U34 AR063407, NIH, PI: Meggan Mackay, MD 09/25/2013 – 9/30/2016
Treatment of SLE with Ajulemic Acid, a Non-Psychoactive Cannabinoid Derivative
Goal: To evaluate the safety of ajulemic acid (AjA) in SLE patients with mild to moderate musculoskeletal pain and to determine an optimum dose of AjA to provide maximum benefit and minimal toxicity.
Role: Director, Biostatistics Unit Overlap: None

Peter Gregersen MD, Key Personnel:

New Active Support: None

New Completed Support
NIH – ACE – 1UM1AI110494-01 Aranow (PI), Gregersen (co-Investigator) 05/01/14 – 04/30/17
The Feinstein Center for Clinical Research in Autoimmune Diseases
The goal is to establish an Autoimmunity Centers of Excellence Basic Science Center.
Role: Co-Investigator

Mathew Bank MD, Co-Investigator (3 calendar months): Nothing to Report

Adam Stein MD, Co-Investigator (0.6 calendar months): Nothing to Report

Site 2: Kessler Foundation

Gail Forrest PhD, Site PI (Kessler):

New Active Support:

New Completed Support:

Steven Kirshblum, MD (Key Personnel, Kessler)

New Active Support:
358004 (Kirshblum, PI) Craig H. Neilsen Foundation 7/31/17 – 7/30/18 0.20 CM (20%)
$181,962 (Total Award) "*Neilsen SCI Medicine Fellowship"*
This Fellowship provides funding for two (2) SCI Clinical Fellow to rotate at Kessler Institutes for Rehabilitation and receive training and support under the supervision of Dr. Steven Kirshblum, Director SCI Clinical Services.

38076 (Kirshblum, PI) Medtronic 7/1/17 – 6/30/18
$20,000 (Total Award) "*SCI Fellowship*: 2017-2018"
This Fellowship provides funding that augments the Craig H. Neilsen Foundation funding for the SCI Fellowship typically utilized for additional travel performed by each Clinical Fellow during the course of their fellowship period.

***Pending Award No. (Rymer, PI)** 9/30/17 – 9/29/22 0.12 CM (1%)
NIDILRR $142,933 (Annual Direct)
"A Multi-Center Clinical Trial to Evaluate the Effectiveness of Intermittent Hypoxia Therapy in Individuals with Spinal Cord Injury"
Role: Co-I
***Have received award notice awaiting official documents from PTE sites.**

New Completed Support:
W81XWH-14-2-0190 (Forrest, PI) 9/30/14 – 9/29/17 0.12 CM (1%)
USAMRAA/CDMRP/DoD *"Testosterone Combined with Electrical Stimulation and Standing: Effect on Muscle and Bone"*
$487,804 (Annual Directs)
$1,834,554 (Total Award)
The major goal of this project is a prospective, randomized, double-blinded, controlled, multi-site clinical trial to determine the effectiveness of a tri combination Activity-Dependent Rehabilitation Model on improving musculoskeletal gains in men with sub-acute to chronic SCI who have low serum testosterone levels.
Role: Co-I

H133A120030 (Chiaravalloti, PI) 10/1/12 – 9/30/17 0.60 CM (5%)
NIDILRR $360,248 (Annual Directs) $2,205,000 (Total Award) *"Northern New Jersey Brain Injury Model Systems"*

The purpose of this award is to contribute to a national database that follows TBI patients from injury through years of follow-up.
Role: Co-I

Site 3: University of Louisville

Max Boakye, MD Site PI (University of Louisville):

New Active Support:
CTN11 Boakye (PI) 6/1/17-5/31/18
Department of Defense/Christopher & Dana Reeve Foundation $72,727
North American Clinical Trials Network (NACTN)
The major goal of this project is to achieve clinical trials capable of indicating effectiveness of promising spinal cord injury (SCI) therapies.

New Completed Support: None

Susan Harkema, PhD Co-Investigator (Louisville):

New Active Support:
ES_BI-2017(Harkema) Harkema (PI) 3/01/2017-2/28/2022 2.4 calendar
Christopher and Dana Reeve Foundation $9,360,000
Task and physiological specific stimulation for recovery of autonomic function, voluntary movement and standing using epidural stimulation and training after severe spinal cord injury.
The major goal of this research is to determine the level of functional gain that can be achieved in voluntary control of movements below the level of injury and autonomic nervous system function as a result of activation of spinal circuits with epidural stimulation with or without task-specific training in humans with complete motor paralysis.

1OT2OD024898-01 Harkema (Co-PI) Hubscher (Co-PI) 09/20/2017-08/31/2020 1.2 calendar
U.S. Army Med Research Acq Activity
Functional Mapping with Lumbosacral Epidural Stimulation
The major goal of this research is improving urogenital function with step training after spinal cord injury.

New Completed Support:

W81XWH14-2-0190 Forrest (PI) Harkema (Co-I) 09/30/14-09/30/17 0.6 calendar
USAMRAA /Kessler Foundation $330,121
Testosterone Combined with Electrical Stimulation and Standing: Effect on Muscle and Bone
The major goal of this research is to investigate the effect of testosterone combined with stand and step (locomotor) training with electrical stimulation of the spinal cord on muscle and bone in individuals who have had a spinal cord injury.

CTN10 Harkema (PI) 06/01/12-05/31/17 0.36 calendar
DOD/Christopher & Dana Reeve Foundation *North American Clinical Trials Network (NACTN)* The major goal of this project is to achieve clinical trials capable of indicating effectiveness of promoting spinal cord injury (SCI) therapies. Role: Principal Investigator, 3%

- **What other organizations were involved as partners?**

There are 3 original organizations collaborating in this study (Sites 1-3). In August, we received permission to add Organizations 4-6 to the study. Execution of subawards with Sites 4-6 is in progress (OSUMC, ICORD/UBC, and Thomas Jefferson), so they are not officially listed here yet, but are referred throughout the document. We expect them to be participating in time to be included in the Year 3 first quarterly technical report.

Organization 1 Name: Feinstein Institute for Medical Research (of Northwell Health)

Location of Organization: *Manhasset, NY*

Partner's contribution to the project *(identify one or more)*

Financial support; Some institutional salary support is provided for the PI and additional study personnel.

In-kind support *(e.g., partner makes software, computers, equipment, etc., available to project staff)* Computers and equipment are available to project staff as needed.

Facilities *(e.g., project staff use the partner's facilities for project activities)*: Facilities are available for the project staff.

Collaboration *(e.g., partner's staff work with project staff on the project)*: This is the site of the overall PI. We have participated in all aspects of study design and tasks included in Major Tasks 1-3.

Organization 2 Name: The Kessler Foundation

Location of Organization: *West Orange, NJ*

Partner's contribution to the project *(identify one or more)*

Financial support:

In-kind support *(e.g., partner makes software, computers, equipment, etc., available to project staff)*; Computers and equipment are available to project staff as needed.

Facilities *(e.g., project staff use the partner's facilities for project activities)*: Facilities are available for the project staff.

Collaboration *(e.g., partner's staff work with project staff on the project)*: Personnel have participated in all aspects of study design and Major Task 1-2. They are hoping to begin Major Task 3 immediately.

Organization 3 Name: University of Louisville

Location of Organization: *Louisville, KY*

Partner's contribution to the project *(identify one or more)*

Financial support:

In-kind support *(e.g., partner makes software, computers, equipment, etc., available to project staff)*; Computers and equipment are available to project staff as needed.

Facilities *(e.g., project staff use the partner's facilities for project activities)*: Facilities are available for the project staff.

Collaboration *(e.g., partner's staff work with project staff on the project)*: Personnel are collaborating on the project. They have participated in all aspects of study design and tasks included in Major Tasks 1-3. This site is actively screening and enrolling participants.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *NOT APPLICABLE-THIS IS A SINGLE PI AWARD.*

QUAD CHARTS: Please see attached.

9. APPENDICES: The modified SOW 20170519 effective 20170815 is attached for easy reference below.

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ADDITIONAL NOTES:

MARKING OF PROPRIETARY INFORMATION: Not applicable.

This generic Statement of Work document is intended to assist applicants with the format preferred by CDMRP. This particular SOW does not contain any specific scientific information and is intended to be easily modifiable for any project. Not all components will be applicable for every project; please consult your Program Announcement for specific award requirements.

STATEMENT OF WORK – REVISED 05/19/2017
START DATE September 30, 2015

Site 1: Feinstein Institute
350 Community Dr,
Manhasset, NY 11030
PI: Bloom, Ona

Site 2: Kessler Foundation
1199 Pleasant Valley Way
West Orange, NJ 07052
Partnering PI: Forrest, Gail

Site 3: University of Louisville
220 Abraham Flexner Way, 11th fl
Louisville, KY 40202
Partnering PI: Boayke, Max

Site 4: Thomas Jefferson University, Partnering PI: Harrop, James

Site 5: ICORD
Partnering PI: Kwon, Brian

Site 6: OSUMC
Partnering PI: Schwab, Jan

Specific Aim 1(specified in proposal)	Timeline	Month, Cal Year	Quarter	Due Date
Major Task 1 Sites 1-3: Obtain IRB and HRPO/ACURO permission for study	1-21	October, 2015-June, 2016	Q1-Q3 Yr 1	6/30/2016
Subtask 1: Submit documents for local IRB* review. with support personnel as indicated in budget justifications	1-3	October-December, 2015	Q1 Yr 1	12/31/15
Subtask 2: Submit IRB approval and necessary documents for HRPO* review. with support personnel as indicated in budget justifications	1-3	October-December, 2015	Q1 Yr 1	12/31/15
Milestone #1 Achieved: HRPO/ACURO Approval	6-21	March-June, 2016	Q2-3 Yr 1	6/30/2016
Sites 4-6: Completion of Major Task 1	22-24	July-Sept, 2017	Q4 Yr 2	9/30/17
Major Task 2 Sites 1-3: Create Infrastructure and Obtain All Supplies/Training for Performance of Outcome Measures	1-6	October 2015-March 2016	Q1-Q2 Yr 1	3/31/2016
Subtask 1: Instruction or Review of Functional Outcome measures: NSLIJHS PT team attends NeuroRecovery Training Institute 2-day training course Review of SCIM scoring criteria with support personnel as indicated in budget	1-6	October 2015-March 2016	Q1-Q2 Yr 1	3/31/2016

justifications				
Subtask 2: non-NRN site personnel visit NRN site(s) for observational case study learning, supervised by Dr. Stein	1-6	October 2015-March 2016	Q1-Q2 Yr 1	3/31/2016
Subtask 3: Create custom clinical database for data entry. Participating Team: led by Dr. Lesser, with feedback from site PIs, with support personnel as indicated in budget justifications	1-3	October-December, 2015	Q1 Yr 1	12/31/15
Subtask 4: Create SOP for clinical team, including data entry forms and instruction on use. Participating Team: Dr. Bloom, in consultation with site PIs	1-3	October-December, 2015	Q1 Yr1	12/31/15
Subtask 5: Send sample collection supplies, SOP and shipping supplies to all sites Site PIs will distribute to relevant local clinical personnel.	4-6	January-March, 2016	Q2 Yr1	6/30/2016
Milestone #2: Infrastructure and Tools obtained needed to begin subject enrollment	6	March, 2016	Q2 Yr1	3/31/2016
Major Task 2 Sites 4-6	22-24	July-Sept, 2017	Q4 Yr 2	9/30/17
Major Task 3 Sites 1-3: Human Subject Study Enrollment	6-45	April, 2016-June, 2019	Q3 Yr 1-Q2 Yr 3	6/30/2019
Subtask 1: Recruit, consent and enroll subjects at acute time points (study visit 1)**.** ***** See quarterly enrollment table, with support personnel as indicated in budget justifications	6-45	April, 2016-June, 2019	Q3 Yr 1-Q2 Yr 3	6/30/2019
Subtask 2: Obtain Biological Samples (blood) from subjects, study visits 1-4 -with clinical and research nursing staff, as needed	6-45	April, 2016-June, 2019	Q3 Yr 1-Q2 Yr 3	6/30/2019
Subtask 3: Process and store biological samples, study visits 1-4	6-45	April, 2016-June, 2019	Q3 Yr 1-Q2 Yr 3	6/30/2019

Subtask 4: Perform ISNCSCI exams and determine AIS grades, study visits 1-4	6-45	April, 2016-June, 2019	Q3 Yr 1-Q2 Yr 3	6/30/2019
Subtask 5: Administer SCIM and determine scores, study visits 2-4, with support personnel as indicated in budget justifications	6-45	April, 2016-June, 2019	Q3 Yr 1-Q2 Yr 3	6/30/2019
Subtask 6: Administer NRS and determine scores, study visits 2-4, with support personnel as indicated in budget justifications	6-45	April, 2016-June, 2019	Q3 Yr 1-Q2 Yr 3D Q3 Yr 1-Q2 Yr 3	6/30/2019
Milestone #3 Achieved: Collection of complete data set from a subset of subjects	6-45	April, 2016-June, 2019	Q3 Yr 2	6/30/2019
Major Task #3 Sites 4-6	22-45	July 2017-June, 2019	Q4 Yr 2	6/30/2019
Major Task #4: Data Analysis, Modeling and Interpretation	31-45	April, 2018-October, 2019	Q3 Yr 3-Q4 Yr 4	
Subtask 1: Pilot Study: Perform biochemical assays on biological samples from subset of subjects (Aim 1) -with support personnel as indicated in budget justifications	31-36	April-June, 2018	Q3 Yr 3	6/30/2018
Subtask 2: Pilot Study: Perform data analysis, statistical modeling and interpretation of data - with support personnel as indicated in budget justifications	31-36	July-Dec, 2018	Q3 Yr 3	12/31/2018
Milestone #3 Achieved: Co-author manuscript on pilot data set	31-36	July-Dec, 2018	Q3 Yr 3	12/31/2018
Subtask 3: Larger/Complete Set of Study Samples: Perform biochemical assays on biological samples from subset of subjects (Aim 1) -with support personnel as indicated in budget justifications	34-48	July, 2018-Sept 29, 2019	Q4 Yr 3-Q4 Yr 4	09/29/2019
Subtask 4: Larger/Complete Set of Study Samples: Perform statistical modeling and interpretation of data - with support personnel as indicated in budget justifications	34-48	July, 2018-Sept 29, 2019	Q4 Yr 3-Q4 Yr 4	09/29/2019

Milestone #4 Achieved: Co-author manuscript on larger/complete data set	34-48	July, 2018-Sept 29, 2019	Q4 Yr 3-Q4 Yr 4	09/29/2019

If human subjects are involved in the proposed study, please provide the projected quarterly enrollment in the following table. Note: The Government reserves the right to request a revised SOW format and/or additional information.

PLEASE SEE PREDICTED ENROLLMENT TABLE ON NEXT PAGE

	Year 1				**Year 2**				**Year 3**				**Year 4**				
Quarter	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**TOTAL**
Month	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	
Year	2015	2016	2016	2016	2016	2017	2017	2017	2017	2018	2018	2018	2018	2019	2019	2019	
Site 1 Feinstein		2	2	0	3	0	0	2	2	3	3	3	3	3	3	0	29
Site 2 Rutgers							1	1	2	3	3	2	2	3	2	0	19
Site 3 Louisville			0	1	1	0	1	1	1	2	2	2	2	2	2	0	17
Site 4 Jefferson	Not yet added to study							2	2	2	2	3	3	2	1	0	17
Site 5 ICORD								0	0	0	2	2	2	2	2	0	10
Site 6 OSMU								1	1	1	1	1	1	1	1	0	8
TOTAL																	100